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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,275	10/28/2003	Bob G. Sanders	CLFR:178USD1	4689

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EXAMINER	
KHARE, DEVESH	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 03/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/695,275	SANDERS ET AL.	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,14-16 and 18-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,14-16 and 18-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/01/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's amendments and remarks filed on 12/01/2005 are acknowledged. Claims 1,2,8,14 and 15 have been amended.

Claims 1-6,8,14-16 and 18-65 are currently pending in this application.

A declaration from Dr. Sanders and Dr. Kline under 37 C.F.R. 1.132 and the prior publications of Lawson et al.; and Zhang et al., have been considered. It is noted that the declaration discloses the effectiveness of compounds comprising an ethylenic R^5 group of claim 1, however the declaration, while being enabling for *in vitro screening* assay to determine the effective concentration of said compounds to induce apoptosis of the cells in culture does not reasonably provide enablement for a method of inhibiting the growth of tumor cells in an individual comprising administering to the individual a pharmacologically effective dose of a compound having structural formula of claim 1.

35 U.S.C. 112, first paragraph rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6,8, 14-16 and 18-65 are rejected under 35 U.S.C. 112, first paragraph, of record, because the specification, while enabling fifteen out of twenty nine RRR-α-tocopherol compounds and two out of five 1-aza-α-tocopherol analogs effective at inducing tumor cells to undergo apoptosis while having no apoptotic inducing properties on normal cells (specification: Example 7, pages 92-93), does not reasonably provide enablement for a method for inhibiting the growth of tumor cells in an individual of claim 1. In the absence of which of the compounds of claim 1 and in the absence of data

disclosing the effectiveness of the compounds of claim 1 **for inhibiting the growth of tumor cells in an individual**, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The factors regarding undue experimentation have been summarized in *In re Wands,* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

(1) The nature of the invention;

(2) The state of the prior art;

(3) The predictability or lack thereof in the art;

(4) The amount of direction or guidance present;

(5) The presence or absence of working examples;

(6) The breadth of the claims;

(7) The quantity of experimentation needed; and

(8) The relative skill of those in the art.

THE NATURE OF THE INVENTION

The nature of the invention in claims 1-6,8, 14-16 and 18-65 is a method for inhibiting the growth of tumor cells in an individual by administering to the individual a pharmacologically effective dose of a compound of claim 1.

THE STATE OF THE PRIOR ART

The instant claimed methods are drawn to a method for inhibiting the growth of tumor cells in an individual by administering to the individual a pharmacologically effective

dose of a compound of claim 1. The following references are cited to show the state of the prior art:

Fariss et al., Cancer Res. 54,3346-51,July1, 1994.

Grisar et al. U.S. Patent 5,545,660.

(the prior art references are provided in the Office Action dated 9/10/2004).

THE PREDICTABILITY OR LACK THEREOF IN THE ART

There would be little predictability in the art of which modifications may be made to a compound of claim 1 wherein X is oxygen or nitrogen and Y is oxygen or NR^6, which would retain its capability to exhibit tumor growth inhibitory properties in an individual. The nature of the pharmaceutical arts is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. In the absence of which Markush groups of the compounds depicted in claim 1 are being effective for the said treatment, there is no umbrella coverage springing forth from the claimed compounds for the said method.

THE AMOUNT OF DIRECTION OR GUIDANCE PRESENT

The structural formula of claim 1 may encompass a great number of compounds having various Markush groups, however, without some guidance as to what specific changes may be made to the instant compound effective for the said treatment, there would be little predictability in making and/or using such compounds. For example, there is no

guidance as to which Markush groups may be selected to the specific compound that would retain its capability to exhibit tumor growth inhibitory properties in an individual. One skilled in the art would not expect any modifications of the instant compound, which is effective for the said method.

THE PRESENCE OR ABSENCE OF WORKING EXAMPLES

The working Examples 1-20 disclose the reduction in tumor growth in mice and in vivo potential for human cancer cells (Example 15).

BREATH OF THE CLAIMS

The breadth of the claims is that a method for inhibiting the growth of tumor cells in an individual by administering to the individual a pharmacologically effective dose of a compound having a general structural formula of claim 1.

THE QUANTITY OF EXPERIMENTATION NEEDED

The quantity of experimentation needed is undue experimentation. One skill in the art would need to determine what listed compounds from a broad selection depicted in claim 1 would be effective to use in a method for inhibiting the growth of tumor cells in an individual.

THE LEVEL OF SKILL IN THE ART

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity **in an individual**. Thus the specification fails to provide sufficient support of the broad use of

the compound having a structural formula of claim 1 because no specific compound is provided. As a result necessitating one of skill to perform an exhaustive search for which compound can be prepared in order to practice the claimed invention.

Genentech Inc. v Novo Nordish A/S (CA FC) 42 USPQ 2d 1001, states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p] atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which compound out of a broad list of Markush groups of claim 1 is effective in the method encompassed in the instant claims, with no assurance of success.

Rejection Maintained

Applicant's arguments filed on 12/01/05 traversing the rejection of claims 1-6,8, 14-16 and 18-65 under 35 U.S.C. 112, first paragraph have been fully considered but they are not persuasive.

Response to Arguments

Applicants argue that "that undue experimentation is not required to practice the invention across the full scope of the compounds in claim 1" and the "declaration and

the attached Exhibits are provided as evidence that the current application is enabling of the methods of the current claims".

The absence of specific disclosures or the correlation of data to support applicant's assertions, invites the skilled artisan to engage in undue experimentation. Although applicant alleges that several researchers have shown prior to the filing of the priority application that chroman ring compounds exhibited anti-proliferative activity (Lawson et al. and Zhang et al.). However, the instant disclosure while being enabling for *in vitro screening* assay to determine the effective concentration of the compounds of claim 1 to induce apoptosis of the cells in culture does not reasonably provide enablement for a method of inhibiting the growth of tumor cells in an individual comprising administering to the individual a pharmacologically effective dose of a compound having structural formula of claim 1.

2. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (571)272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang, Supervisory Patent Examiner, Art Unit 1623 can be reached at (571)272-0627. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Devesh Khare, Ph.D.,J.D.
Art Unit 1623
February 27, 2006

3/1/06
Anna Jiang, Ph.D.
Supervisory Patent Examiner
Technology Center 1600